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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,553	11/28/2000	Peter S. Lu	020054001130	7232

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EXAMINER
BELYAVSKYI, MICHAIL A

ART UNIT	PAPER NUMBER
1644	17

DATE MAILED: 07/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,553	LU ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-8,16 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-8,16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 May 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Michail Belyavskyi, Art Unit 1644, Technology Center 1600.

2. Applicant's amendment, filed 5/5/03 (Paper No. 16), is acknowledged.

Claims 1, 5-8 and 16-17 are pending.

Claims 1, 5-8 and 16-17 are under consideration in the instant application.

In view of the amendment, filed 5/5/03 (Paper No. 16) the following rejection remains

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-8 and 16-17 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the same reasons set forth in the previous Office Action, Paper No: 13, mailed 11/04/02.

Applicant's arguments, filed 5/05/03 (Paper No. 16), have been fully considered, but have not been found convincing.

Applicant asserts that : (i) LPAP and TIP-1 are expressed in all endothelial or hematopoietic cells, as evidenced by Ding et al and by the search of human ESTs corresponding to TIP-1; (ii) that one of ordinary skill in the art can predict without undue experimentation which agent have inhibitory activity and that specification provides significant information to guide one of ordinary skill in the development of appropriate inhibitory agents and (iii) there are two

examples that illustrate the general strategy that one would employ to identify an inhibitor of a particular PDZ and PL pair.

Contrary to the Applicant's assertion the issue raised by the examiner was that the specification does not disclosed that a particular PDZ/PL pair that is LPAP protein / TIP-1 protein is expressed in any endothelial or hematopoietic cells. Moreover, Applicant himself acknowledge that vast majority of PDZ proteins are not known to be expressed in immune system (see page 29, lines 19-23 in particular). In addition, the specification disclosed that PL proteins are not constantly present in the cells but rather expressed or upregulated only under certain conditions or in certain cell types (see page 37, lines 9-13). Additionally, the specification disclosed that PDZ proteins are differentially expressed in various endothelial or hematopoietic cells, for example, INADLZ/3 can be detected only in T cells but not in B cell. Moreover, the specification also disclosed that there are a numerous PDZ/PL interactions that are occurring in cell of the hematopoietic system (see page 97, line 7-11 in particular). However, there is no teaching in the specification which of this numerous interaction are important for any specific biological function and inhibition of which specific PDZ/PL binding would modulate said biological function. Therefore, it would require undue experimentation for one of skill who wanted to practice the claimed method to determine specific type of the cell in which a specific PDZ /PL pair is expressed and regulate a specific biological function that can be modulated by inhibiting binding of a specific PDZ protein to specific PL protein. Ding et al. only teach that LPAP gene was inactivated in a particular subpopulation of lymphatic cells, in T lymphocyte in particular, thus providing evidence that LPAP expressed only in T lymphocytes not in any endothelial or hematopoietic cells.

Also, the issue raised by the examiner was not if one of ordinary skill in the art can develop or identify an inhibitor of a particular PDZ and PL pair. Rather the issue was that since the function of LPAP is unknown (as disclosed on page 111, lines 21-25 of the specification as filled and taught by Ding et al.) how can one of ordinary skill in the art predict which biological function of an endothelial cell or hematopoietic cells would be modulated by introducing into the cell an agent that inhibits binding of LPAP with TIP1? Therefore, it would require undue experimentation for one of skill who wanted to practice the claimed method to determine which (if any) of the biological function of an endothelial cell or hematopoietic cell would be modulated by inhibiting interaction of LPAP/TIP1 pair. Moreover, the exemplifications in the specification are drawn to general strategy that one would employ to identify an inhibitor for a particular PDZ/PL pair in *in vitro* assay "A" or assay G". Since there is no animal model system in the specification that shows modulation of any biological function of an endothelial or hematopoietic cell, after introducing into the cell an agent that inhibits binding of a particular PDZ/PL pair, it is unpredictable how to correlate test tube results with in vivo clinical trial. Since the method of modulation a biological function of an endothelial cell or hematopoietic cells can be species- and model-dependent, it is not clear that reliance on the test tube studies accurately reflects the relative human efficacy of the claimed therapeutic strategy. The specification does not adequately teach how to effectively modulate a biological function of an endothelial cell or hematopoietic cells by introducing into the cell an agent that inhibits binding of LPAP with TIP1. The specification does not teach how to extrapolate data obtained from *in*

vitro studies to the development of effective *in vivo* mammalian including human therapeutic treatment, commensurate in scope with the claimed invention. It addition, Bals R., et al., (Infection and Immunity, 1999, v.67, pages 6084-6089) teach that functional studies have been restricted primarily to *in vitro* experiments with purified peptides and do not necessarily reflect the complexity of *in vivo* interaction, such as synergism and antagonism between individual substances (see overlapping pages 6087-6088 in particular).

The following new ground of rejection is necessitated by the amendment filed 5/5/03 (Paper No. 16).

4. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 5 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5 and 6 are indefinite and ambiguous in being dependent upon canceled claims 2 and 4 accordingly.

6. No claim allowed

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
July 14, 2003.

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600